

2. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

- (a) encodes the amino acid sequence shown in SEQ ID NO:2; and
- (b) hybridizes to the nucleotide sequence of SEQ ID NO:1 or the complement thereof under highly stringent conditions of 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

4. (Amended) An isolated expression vector comprising a nucleic acid molecule that comprises the nucleotide sequence of SEQ ID NO:1.

Please add new claims 5 and 6 as follows:

--5. (New) An isolated expression vector comprising a nucleic acid molecule that encodes the amino acid sequence described in SEQ ID NO:2.

6. (New) A host cell comprising the expression vector of claim 4 or 5.--

RESPONSE

I. Status of the Claims

No claims have been canceled. Claims 1, 2 and 4 have been amended. New claims 5 and 6 have been added.

Claims 1-6 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**. In compliance with 37 C.F.R. § 1.121(c)(1)(ii), a marked up copy of the original claims is attached hereto as **Exhibit B**.

II. Support for the Amended and Newly Added Claims

Claim 1 has been amended to recite that the isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in claim 1 as originally filed and in Section

5.1.

Claim 2 has been amended to recite specific highly stringent hybridization conditions. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least on page 5, lines 2-12.

Claim 4 has been amended to recite that the isolated expression vector comprises the nucleotide sequence of SEQ ID NO:1. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in claim 4 as originally filed.

Claim 5 has been added to specifically recite an expression vector comprising a nucleic acid molecule that encodes the amino acid sequence described in SEQ ID NO:2. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in claim 4 as originally filed and on page 15, lines 5-12.

Claim 6 has been added to specifically recite host cells comprising the expression vector of claim 4 or 5. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least at page 15, lines 12-18.

It will be understood that no new matter is included within the amended or newly added claims.

III. Rejection of Claims 1-4 Under 35 U.S.C. § 101

The Action first rejects claims 1-4 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

The present invention has a number of substantial and credible utilities, not the least of which is, as described in the specification on page 6, lines 16-18, that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. As the present sequences are specific markers of the human genome, and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such DNA chips. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, as described in the specification at least at page 3, lines 7-12, the present nucleotide sequence has a specific utility in mapping the protein encoding regions of the corresponding human chromosome, specifically chromosome 1. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 1 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Applicants respectfully remind the Examiner that only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. The present invention expands the utility of data coming from the human genome project. Persons of skill in the art, as well as thousands of venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. All current therapeutics used in humans directly or indirectly interact with biological sequences encoded by the human genome, and virtually all future human therapeutics shall do likewise.

Consequently, billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, *Science* 291:1304). The results have been a stunning success, as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, *Science* 291:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years). The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

As set forth by the Federal Circuit, “(t)he threshold of utility is not high: An invention is ‘useful’ under section 101 if it is capable of providing some identifiable benefit.” *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that “(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result.” *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); “*Cross*”) states “any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101”. *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that “anything under the sun that is made by man” is patentable (*State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

In *In re Brana*, (34 USPQ2d 1436 (Fed. Cir. 1995), “*Brana*”), the Federal Circuit admonished the P.T.O. for confusing “the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption”. *Brana* at 1442. The Federal Circuit went on to state:

At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase “utility or usefulness” in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using “utility” to refer to rejections under 35 U.S.C. § 101, and is using “usefulness” to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. Even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit’s holding in *Brana*, which clearly states, as highlighted in the quote above, that “pharmaceutical inventions, necessarily includes the expectation of further research and development” (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is “undue”, not “experimentation”. *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra; Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The Action states that the invention lacks utility because the disclosure does not provide a “demonstrated function for the protein of SEQ ID NO:2” (Action at page 2, emphasis added). This argument also fails, because it has long been established that “there is no statutory requirement for the disclosure of a specific example”. *In re Gay*, 135 USPQ 311 (CCPA 1962).

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office (“the PTO”) itself for

compliance with 35 U.S.C. § 101. While Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the “real-world” utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section V, below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1-4 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

IV. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects claim 2 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

The Action rejects claim 2 as allegedly indefinite based on the term “highly stringent hybridization conditions”, because the specific hybridization and washing conditions are not recited in the claim. While Applicants submit that the term is sufficiently definite, as a number of stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance the claim has been revised to recite specific highly stringent hybridization conditions. As the specification provides specific teaching regarding these highly stringent hybridization conditions, at least on page 5, lines 2-12, Applicants submit that revised claim 2 even more clearly meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants therefore request withdrawal of this rejection.

V. Rejection of Claims 1-4 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1-4 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-4 have been shown to have “a specific, substantial, and credible utility”, as detailed in section III above, the present rejection of claims 1-4 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1-4 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VI. Rejection of Claims 1 and 4 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1 and 4 under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for the full scope of the claimed invention comprising a genus of at least 60 contiguous nucleotides of SEQ ID NO:1. While Applicants in no way agree that the present application does not provide enablement for nucleotide sequences comprising at least 60 contiguous

nucleotides from SEQ ID NO:1, as claims 1 and 4 currently recite only nucleic acid molecules comprising the nucleotide sequence of SEQ ID NO:1, which is clearly enabled, the present rejection of claims 1 and 4 under 35 U.S.C. § 112, first paragraph, has been rendered moot. Applicants therefore respectfully request that the rejection of claims 1 and 4 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VII. Rejection of Claims 1 and 4 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1 and 4 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Again, while Applicants in no way agree that the present application does not provide sufficient written description for nucleotide sequences comprising at least 60 contiguous nucleotides from SEQ ID NO:1, as claims 1 and 4 currently recite only nucleic acid molecules comprising the nucleotide sequence of SEQ ID NO:1, which the Action admits is disclosed in the specification (Action at page 6), the present rejection of claims 1 and 4 under 35 U.S.C. § 112, first paragraph, has been rendered moot. Applicants therefore respectfully request that the rejection of claims 1 and 4 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VIII. Rejection of Claims 1 and 4 Under 35 U.S.C. § 102(b)

The Action next rejects claims 1 and 4 under 35 U.S.C. § 102(b), as allegedly anticipated by Fujiwara *et al.* (1996, GenBank Database Accession No. D78761; “D78761”) or NCI-CGAP (1999, Accession Number AI637480; “AI637480”). While Applicants do not necessarily agree with the present rejection, as claims 1 and 4 have been amended to recite the complete nucleotide sequence of SEQ ID NO:1, which is neither taught nor suggested by D78761 or AI637480, Applicants submit that the rejection of claims 1 and 4 under 35 U.S.C. § 102(b) has been overcome, and respectfully request withdrawal of the rejection.

IX. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Swope have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

November 12, 2002

Date



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